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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,564	08/28/2006	Peter Richardson	13425-170US1	4551

26161 7590 05/15/2009
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EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
05/15/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/537,564	RICHARDSON, PETER	
	Examiner	Art Unit	
	Lawrence E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 19, 2009 (Response)*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-14,16,17,19-31 and 47-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14, 16, 17, 19-31 and 47-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims **1-10, 15, 18 and 32-46** were previously cancelled, no claims have been newly cancelled, no claims have been amended, the disclosure has not been amended further, and no new claims have been added as per the response filed February 19, 2009. No additional or supplemental Information Disclosure Statements (IDSs) have been received as of the date of this Office action. Two references supplied by applicant have been made of record on an updated PTO-892. In addition, complete copies of PTO-892 references **T and U** have becom available and have been supplied herewith.

Claims **11-14, 16, 17, 19-31 and 47-52** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **47-50** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Factors to be considered:

a) Actual Reduction to Practice? In the instant disclosure there are no examples wherein applicant has demonstrated that pre-injury administration of spongosine, or spongosine plus gabapentin, is effective in suppression of pain (inducing analgesia) in a host expected to be in need thereof.

b) Disclosure of Drawings or Structural Chemical Formulas? This factor is not applicable in this case.

c) Sufficient relevant identifying characteristics? This factor is not applicable in this case.

d) Method of making the claimed invention? This factor is not applicable in this case.

e) Level of skill in the art? This factor is not applicable in this case.

f) Predictability in the art? The absence of appropriate data makes predictability impossible to access and therefore this is an important consideration in this case.

The lack of appropriate test data, and therefore the impossibility of accessing predictability, support the conclusion that the instant claims are directed to subject matter not in applicant's possession as of the date the instant case was filed. For this reason applicant is respectfully requested to cancel the noted claims, or to take other appropriate action.

Applicant's arguments with respect to claims **47-50** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

Claims **11-14, 16, 17, 19-31 and 47-52** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for the treatment of inflammation, hypertension, and pain by the administration of spongosine, or a combination of spongosine and the amino acid gabapentin, does not reasonably provide enablement for the treatment of any of the noted conditions with any other mixtures of spongosine and another analgesic agent as disclosed in claims **27 and 28**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The instant claims are directed to the treatment of pain by administration of spongosine or spongosine plus an additional analgesic agent without defining the particular additional analgesic agent in other than generic or subgeneric terms. The claims are therefore deemed to be excessively broad in scope.

B. The nature of the invention: The invention defined by the listed claims is directed to the treatment of pain by the administration of a 2-methoxyadenosine, alone or in combination with a second analgesic compound, to a host in need thereof.

C. The state of the prior art: Instant prior art identifies the claimed active ingredient and also identifies analgesic pharmacological activity in adenosine and numerous other adenosine analogues. It is also argued in another rejection that the instant claimed method is anticipated when inflammation caused by an irritant (carrageenan), and the presumed pain accompanying said inflammation, is effectively treated by the administration of spongosine in light of its antiinflammatory and analgesic properties.

D. The level of one of ordinary skill: One of ordinary skill would be expected to be familiar with the details of the medicinal treatment of pain and also familiar with the possibility of dangerous (and possibly fatal) synergisms sometimes observed when administrating multiple analgesic substances simultaneously.

E. The level of predictability in the art: In view of the absence of teachings herein and in the prior art to provide relevant guidance directed to determining in advance what are safe and what are unsafe combinations of analgesics with spongosine, the safety of the combinations of spongosine with other analgesics is highly unpredictable.

F. The amount of direction provided by the applicant: The instant disclosure, as noted above, only supplies two and one-half pages of guidance and an indication of how to treat pain associated with only a few model test hosts wherein the pain has been induced artificially. And in addition, the examples only include one example wherein a combination of spongosine with the additional analgesic gabapentin are tested, and no guidance concerning how to safely select the "other" possible analgesics as disclosed generically and subgenerically in claims **27 and 28**.

G. The existence of working examples: The existence and the content of examples is described in previous paragraphs.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because the bare minimum of examples in the instant disclosure at pages 7-9 is entirely inadequate to provide the guidance necessary to practice the instant claimed method for the treatment of pain by the administration of spongosine alone, or in combination with another analgesic, without undue experimentation.

Applicant's arguments filed February 19, 2009 have been fully considered but they are not persuasive.

Examiner notes that in claim **11** the term "comprises" effectively means that, should this claim be allowed, applicant would have the right to claim infringement by any claim granted to another wherein spongosine is administered to treat pain. Therefore, instant claims **27-28**, except wherein gabapentin is the second analgesic, are superfluous because applicant would not be denied the infringement right for claims wherein mixtures of analgesics including spongosine are administered as noted above.

Applicant's arguments have failed to cite two decisions that bear on the instant subject matter: *Ex parte Balzarini* (21, USPQ 2d 1892, 1894 (BPAI, 1991)) and *In re Jolles* (628 F. 2d 1322; 206 USPQ 885 (CCPA 1980)).

Ex parte Balzarini et al. in its first opinion stands for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art areas are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of the efficacy of the alleged treatment. See MPEP at §2107.03. The applicant asserted that a compound that looked like AZT would be reasonably expected to have similar anti-HIV activity without supporting test data, an assertion found unconvincing by the PTO BPAI.

In re Jolles (628 F. 2d 1322; 206 USPQ 885 (CCPA 1980)) stands for the proposition that relevant and believable test data showing that analogues of a known anticancer compound have similar anti-cancer activity are effective in establishing the utility of the analogue compounds as anti-cancer compounds. See MPEP at §2107.01.

The administration of a medicinally active substance to a host in need thereof is subject to a heightened standard of enablement that the decisions cited by applicant do not address, but which is addressed in the MPEP particularly at §2107.01-2107.03.

It is examiner's view that applicant is attempting to extrapolate to a much larger subject matter area without appropriate test data to support the extrapolation. As suggested by examiner to applicant's representative in a recent interview, additional data would provide

more enabling support and thereby provide the more extensive foundation needed to extend the scope of enabled subject matter.

For these reasons the above ground of rejection has been maintained.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **11-14, 16, 17, 19-31 and 47-52** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***16-33*** of copending Application No. **10/547,455**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of treatment both appear to include or imply the treatment of pain and the alleged active ingredients (2-alkoxyadenosines and their 3'-deoxy analogues) are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed February 19, 2009 have been fully considered but they are not persuasive.

Applicant has acknowledged the instant rejection but has not yet supplied the requested Terminal Disclaimer. Therefore,. the instant rejection has been maintained.

Claims **11-14, 16, 17, 19-31 and 47-52** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***13-24*** of copending Application No. **10/547,454**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods of treatment both appear to include or imply the treatment of pain and the alleged active ingredients (2-alkoxyadenosines and their 3'-deoxy analogues) are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed February 19, 2009 have been fully considered but they are not persuasive.

Applicant has acknowledged the instant rejection but has not yet supplied the requested Terminal Disclaimer. Therefore,. the instant rejection has been maintained.

Claims **11-14, 16, 17, 19-31 and 47-52** of this application conflict with ***13-24*** of copending Application No. **10/547,454** and ***16-33*** of copending Application No. **10/547,455**. 37 C.F.R. §1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP §822.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claims **11-14, 16, 17, 19-31 and 47-52** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Bartlett et al.** (PTO-1449 ref. **AN**).

Applicant is referred to Table I at page 949 and associated explanation at page 950, column 1, fifth full paragraph, wherein the administration of spongosine, compound numbers "**18**," to treat carrageenan induced inflammation must have inherently included suppression of pain in the hosts so treated, thereby anticipating the instant claimed subject matter. The allegation of inherency is supported by the definition of "inflammation" in Taber's Cyclopedic Medical Dictionary, 19th Ed. (2001) at page 1092, column 1, wherein the occurrence of "inflammation" is defined to include the simultaneous occurrence of "pain" and other symptoms (see PTO-892 ref. **X**).

Applicant's arguments filed February 19, 2009 have been fully considered but they are not persuasive.

Applicant cites the definition of "edema" in Taber's Cyclopedic Medical Dictionary (now made of record as PTO-892 ref. **V**) and in the paragraph bridging pages 5 and 6 of the response asserts that "[n]owhere does this definition [of "edema"] recite pain, or state that pain is a required or necessary component of edema." Examiner resp[ectfully disagrees, noting at pages 665-666 that "inflammatory edema" is [e]dema associated with inflammation" and is "usually ... localized, and red, tender and warm," wherein the term "tender" clearly teaches that edema and pain are associated.

In order to make the documentary record more complete, examiner has made of record the Taber's Cyclopedic Medical Dictionary definitions of both "inflammation" and "pain" as PTO-892 ref. **X**.

In addition, examiner notes that the term "edema" is cited by applicant but that the term "inflammation" is found repeatedly in the **Bartlett et al.** reference. Examiner also notes that Taber's defines inflammation as "[a]n immunological defense against injury, infection, or allergy ... " wherein the "... clinical hallmarks are redness, heat, swelling, pain, and loss of function of a body part." The overlap between the cited definitions of inflammation of edema suggests that the above rejection remains valid, particularly in view of the high likelihood that the injury and/or allergic inflammatory reaction cased by caarageenan injection is accompanied by pain. The presence of the single step of administration of spongosine and the consequent amelioration of edema and associated inflammation is presumed to include amelioration of the associated pain as well.

For the above reasons the above rejection has been maintained.

The previous obviousness rejection citing the two applications cited above in obviousness-type double patenting rejections has been withdrawn in view of applicant's arguments, arguments found convincing by examiner.

The following is a quotation of 35 U.S.C. §103**(a)** which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **11-14, 16, 17, 19-31 and 47-52** are rejected under 35 U.S.C. §103**(a)** as being unpatentable over **Bartlett et al.** (PTO-1449 ref. **AN**) in view of **Herrick-Davis et al.** (PTO-892 ref. **T**).

The instant claims are directed to methods of treatment wherein 2-methoxyadenosine is administered to treat pain.

Bartlett et al. discloses that spongosine (compound "3a") is an effective agent to treat inflammation caused by contact of a test host with carrageenan. Because inflammation is defined to include "redness," "heat," "swelling," "pain," and "loss of function" (Taber's Cyclopedic Medical Dictionary, 19th Ed., 2001, at page 1092, column 1; see PTO-892 ref. **X**), and in view of the effectiveness of the administration of spongosine to treat inflammation according to this reference, examiner concludes that it is inherent that spongosine was effective in the treatment of all of the hallmarks of inflammation, including pain.

The **Bartlett et al.** reference did not specifically disclose the testing of spongosine to determine its analgesic activity.

Herrick-Davis et al. discloses that a variety of adenosine analogues that are also known in the art to be adenosine receptor agonists have been found to be analgesic agents with efficacy comparable to morphine. One of the compounds tested, 2-chloroadenosine (CADO), is a close structural relative to spongosine.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to conclude that compounds very closely analogous to CADO disclosed to be a potent analgesic by **Herrick-Davis et al.** to be consistent with an analgesic effect of spongosine as disclosed by **Bartlett et al.** in the treatment of an inflammatory response.

One having ordinary skill in the art would have been motivated to combine these references because both references are directed to disclosures of the analgesic effects observed following the administration of 2-substituted analogues of adenosine, including one compound (spongosine) defined herein as an active ingredient effective in the treatment of pain and/or inflammation inflammation.

Therefore, the instant claimed methods of administration of 2-methoxyadenosine (aka spongosine) to treat pain and/or inflammation would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

Applicant's arguments filed February 19, 2009 have been fully considered but they are not persuasive.

Applicant is referred to the arguments above following the anticipation rejection as relevant to applicant's argument in re inherency and the overlapping medical dictionary definitions of "edema," "inflammation" and "pain."

Examiner respectfully suggests that the secondary reference, **Herrick-Davis et al.**, has additional support in the form of the previously cited **Fukunaga** patent reference, the newly cited **Fukunaga** patent references, and the newly cited **Sollevi** patent references, all of which disclose that adenosine has been established to have analgesic activity, an activity identified as very useful in the **Fukunaga** disclosures for the purpose of inducing simultaneous anesthesia and analgesia by the controlled administration of adenosine to a host in need thereof. Thus, the question of a correlation between analgesic activity and 2-substitution in adenosine and adenosine analogues suggests that small 2-substituents may not have much effect on the analgesic activity of adenosine, and therefore that 2-substituted analogues of adenosine can be reasonably expected to have analgesic activity similar to that of adenosine itself.

For the above reasons the above rejection has been maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

LECrane:lec
05/06/2009

/Lawrence E. Crane/

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